

DATA EVALUATION RECORD

STUDY 3

PM

CHEM 182976

UNICONAZOLE

162-1

BRANCH EAB

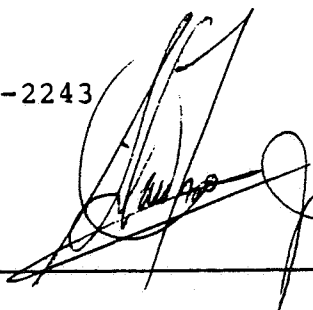
FORMULATION 00-Radiolabeled Active Ingredient

- a. EPA MRID No. 40345428. Itoh, K., Nambu, K., Mikami, N., Matsuda, T., and Miyamoto, J. 1986. Degradation of S-3307D in soils under aerobic upland conditions. Performed by Sumitomo Chemical Company. Laboratory Project Identification IIM-60-0007. Completed December 17, 1986. Submitted by Chevron Chemical Company, Richmond, CA.
- b. EPA MRID No. 40573602. Crisp, C.E. 1988. Comparison of two Japanese soil types to typical U.S. soils. Reply to the EPA's comments of the reports entitled: 1. Degradation of S-3307D in soils under aerobic upland conditions; 2. Adsorption and desorption of S-3307D in water-soil suspension systems; 3. Leaching behavior of S-3307D in soil. Performed and submitted by Chevron Chemical Company, Richmond, CA. Completed March 25, 1988.

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CONCLUSIONS:

The aerobic soil metabolism study is acceptable and fulfills data requirements for the aerobic soil metabolism of uniconazole. The study was conducted with two Japanese soils. These soils were shown (MRID No. 40573602) to be equivalent to United States soils. Under the United States soil classification, the Japanese soils (Kuki and Azuchi) have a sandy loam texture.

Each of the four isomers [(R)-E-; (S)-E-; (R)-Z-, and (S)-Z-] were aerobically incubated over a 12-month period. The degradation rates followed the order (R)-Z->(S)-Z->(S)-E->(R)-E-. The half-life for uniconazole (i.e., the (S)-E-isomer) was calculated as 390 days. The half-life values for the other isomers were 415, 60, and 2 days for (R)-E-, (S)-Z-, and (R)-Z-isomers, respectively.

At least nine degradation products were identified. Some of the degradation products were unique to the E and Z isomers. For the (S)-E-isomer, the predominant degradation product was 1-(4-chlorophenyl)-4,4-dimethyl-2-(1,2,4-triazol-1-yl)-1,2-epoxypentan-3-ol (< 1.5% of applied after 12 months). ¹⁴C-¹⁴CO₂-evolution was between 2.4 and 5.4% of the applied, depending on the soil. It was found that bound residues increased with time.

The proposed degradation pattern for the E-isomers was epoxidation of the 1,2-double bond, with no significant E/Z isomerization or R/S epimerization. For the Z-isomers, oxidation of >CHOH to >C = O and reduction at the 1,2-double bond were major degradation pathways.

- a. MRID No. 40345428. Itoh, K., Nambu, K., Mikami, N., Natsuda, T., and Miyamoto, J. 1986. Degradation of S-3307D in soils under aerobic upland conditions. Performed by Sumitomo Chemical Company. Laboratory Project Identification IIM-60-0007. Completed December 17, 1986. Submitted by Chevron Chemical Company, Richmond, CA.

MATERIALS AND METHODS

Test materials: The E-isomers and the Z-isomers, each one with the corresponding (R)- and (S)-optical isomer, separately labeled in the phenyl ring (phenyl- ^{14}C) and in the triazolyl ring (trz- ^{14}C). The structures and radiochemical and optical purities of each isomer are shown in Table I. Reference compounds were also prepared (Table II).

Soils: Two Japanese loam soils (Kuki and Azuchi) were used. Their characteristics are summarized in Table III.

Procedure: The soils were sieved through a 2-mm mesh. Then, 30 g of soil (dry basis) were moistened (distilled water) to 75% of 0.33 bar moisture and incubated at $25 \pm 2^\circ\text{C}$ in the dark for two weeks. After incubation, each ^{14}C -isomer in benzene (100 μL) was added separately to the soils (0.50-0.77 ppm or 3.8-4.0 μCi relative to dry soil) and the soil samples were placed in 3-L brown glass jars, covered with aluminum foil, and kept at $25 \pm 2^\circ\text{C}$ in a temperature controlled room for 12 months. Each jar was continuously purged with CO_2 -free air (25-30 mL/min). The effluent gas was passed through NaOH and polyurethane foam traps, as shown in Figure 1. Soil moisture content was maintained by periodical additions of distilled water.

Analytical methods

Volatile ^{14}C : NaOH traps and polyurethane foams were radioassayed after extraction with methanol. $^{14}\text{CO}_2$ was determined by precipitation with BaCl_2 and subsequent radioassaying as $\text{Ba}^{14}\text{CO}_3$.

Soils were sampled at 1, 3, 7, 14 days, 1, 2, 3, 4, 6, 9, and 12 months post-treatment. The soil samples were extracted 3-times with methanol (70 mL); each extraction was followed by centrifugation.³ The combined methanol extracts were radioassayed, concentrated in a rotary vacuum evaporator, and the residues redissolved in methanol. TLC-silica gel plates were used to separate the reaction products. The solvent systems used were Solvent A, benzene/acetone:3/1; Solvent B, toluene/ethylformate/formic acid:5/7/1; Solvent A for the first direction and

Solvent C (chloroform/methanol:15/1) for the second direction.

Bound ^{14}C residues were fractionated into fulvic acid, humic acid, and humin fractions. The fulvic acid fractions were radioassayed (AquasolTM-2) and the humic acid and humin fractions were analyzed by LSC after combustion.

Organosoluble fractions, ^{14}C regions scraped from TLC plates, and aqueous solutions (after addition of AquasolTM-2) were analyzed by LSC.

Parent and degradation products were confirmed by HPLC with a UV monitor and a radioanalyzer in series.

Reported results

The recovery of each isomer immediately after application at an application rate of 0.5 ppm was, in all cases, >89%.

The decline curves for each isomer are shown in Figure 2. The half-lives for the disappearance of each isomer in the Kuki and Azuchi soils (computed by a least-square method) are shown in Table IV. The faster degradation occurred with the Z-isomers, which ranged from 2-271 days in contrast with 390-528 days for the E-isomers. After 368-day incubation, the amount of (E)-isomers was 59.0-61.6% and 53.5-56.7% of applied in Kuki and Azuchi soils, respectively while for the (Z)-isomers it ranged from 23.9-45.9% for the (S)-Z-isomer and from 1.0-1.3% for the (R)-Z-isomer. The degradation rates can be summarized as (R)-Z- > (S)-Z- > S-E- > (R)-E-.

Degradation products: At least nine products were present in the methanol extracts. Little difference was found in the TLC plates of the phenyl- ^{14}C and trz- ^{14}C preparations. The identified products were 7KE, 7KZ, 7SK, 7EP, and 7SA. The latter two degradates were unique to the E and Z isomers, respectively. No R/S epimerization was observed with the E-isomers and the (S)-Z-isomer during the course of the experiments. However, with the (R)-Z-isomer, epimerization to the (S)-Z-isomer was detected 30 days after treatment. Other minor products were detected, which were not identical with the derivatives of E- or Z- isomers hydroxylated at the tert-butyl group or at the 2- or 3- position in the phenyl group. Degradation products and their amounts are presented in Tables V-XVI. Small amounts of $^{14}\text{CO}_2$ were detected in soils treated with the phenyl- ^{14}C preparations. Bound residues increased with time (26.3-45.6% of the applied after 348 days) and were in larger amounts with the trz- ^{14}C preparations. The bound ^{14}C was mainly associated with the fulvic acid fraction in Kuki soil and with the fulvic acid and humin fractions of the Azuchi soil.

The proposed degradation pattern is shown in Figure 3. The main pathway of the E-isomers was epoxidation of the 1,2-double bond, with no significant E/Z isomerization or R/S epimerization. For the Z-isomers, oxidation of >CHOH to >C=O and reduction at the 1,2-double bond were major degradation pathways.

The authors indicated that the results suggest that cleavage of C-C and/or C-N bonds occurs between the phenyl and triazolyl rings.

Reviewer's Comments

This study may be acceptable if the registrant can clearly and conclusively demonstrate that the Japanese soils used in the studies are equivalent to soils in the United States.

- b. EPA MRID No. 40573602. Crisp, C.E. 1988. Comparison of two Japanese soil types to typical U.S. soils. Reply to the EPA's comments of the reports entitled: 1. Degradation of S-3307D in soils under aerobic upland conditions; 2. Adsorption and desorption of S-3307D in water-soil suspension systems; 3. Leaching behavior of S-3307D in soil. Performed and submitted by Chevron Chemical Company, Richmond, CA. Completed March 25, 1988.

The soils (Kuki and Azuchi), which in the Japanese system classify as loam soil, can be classified as sandy loam soils under the United States System. The characteristics of Japanese soils were compared with a wide variety of U.S. soils (data taken from the U.S. Department of Agriculture. 1975. Soil Taxonomy - A basic system of soil classification for making and interpreting soil surveys, Soil Conservation Service, U.S.D.A., Agriculture Handbook No. 436, U.S. Printing Office; 1975 0-470-728, pp. 1-754).

The U.S. soils compared with the Japanese soils (pH, cation exchange capacity, organic content, sand/silt/clay-content). Therefore, the data obtained from the aerobic soil metabolism study using Japanese soils can be made acceptable to fulfill data requirements for aerobic soil metabolism studies of uniconazole.